

SEQUENCE LISTING

<110> NAKAGAWARA, Akira
OZAKI, Toshinori

<120> METHOD OF SCREENING COMPOUND CAPABLE OF ACCELERATING OR INHIBITING
APOPTOSIS, APOPTOSIS ACCELERATOR AND APOPTOSIS INHIBITOR

<130> Q97365

<150> JP 2004-93,266

<151> 2004-03-26

<150> JP 2004-176,107

<151> 2004-06-14

<160> 26

<170> PatentIn version 3.1

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cttgcccaa	gggtttcaga	gaaaggactg	tggacctcta	tcattctgcta	agtaatttag	3480
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 <212> PRT

<213> Homo sapiens

<400> 24

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Gln His Arg Glu Leu Asp Leu Lys Ile Ala Ile Lys Ser Cys Arg Leu
35 40 45

Glu Leu Ser Thr Lys Asn Arg Glu Arg Trp Cys His Glu Ile Gln Ile
50 55 60

Met Lys Lys Leu Asn His Ala Asn Val Val Lys Ala Cys Asp Val Pro
65 70 75 80

Glu Glu Leu Asn Ile Leu Ile His Asp Val Pro Leu Leu Ala Met Glu
85 90 95

Tyr Cys Ser Gly Gly Asp Leu Arg Lys Leu Leu Asn Lys Pro Glu Asn
100 105 110

Cys Cys Gly Leu Lys Glu Ser Gln Ile Leu Ser Leu Leu Ser Asp Ile
115 120 125

Gly Ser Gly Ile Arg Tyr Leu His Glu Asn Lys Ile Ile His Arg Asp
130 135 140

Leu Lys Pro Glu Asn Ile Val Leu Gln Asp Val Gly Gly Lys Ile Ile
145 150 155 160

His Lys Ile Ile Asp Leu Gly Tyr Ala Lys Asp Val Asp Gln Gly Ser
165 170 175

Leu Cys Thr Ser Phe Val Gly Thr Leu Gln Tyr Leu Ala Pro Glu Leu
180 185 190

Phe Glu Asn Lys Pro Tyr Thr Ala Thr Val Asp Tyr Trp Ser Phe Gly
195 200 205

Thr Met Val Phe Glu Cys Ile Ala Gly Tyr Arg Pro Phe Leu His His
210 215 220

Leu Gln Pro Phe Thr Trp His Glu Lys Ile Lys Lys Lys Asp Pro Lys
 225 230 235 240

Cys Ile Phe Ala Cys Glu Glu Met Ser Gly Glu Val Arg Phe Ser Ser
 245 250 255

His Leu Pro Gln Pro Asn Ser Leu Cys Ser Leu Ile Val Glu Pro Met
 260 265 270

Glu Asn Trp Leu Gln Leu Met Leu Asn Trp Asp Pro Gln Gln Arg Gly
 275 280 285

Gly Pro Val Asp Leu Thr Leu Lys Gln Pro Arg Cys Phe Val Leu Met
 290 295 300

Asp His Ile Leu Asn Leu Lys Ile Val His Ile Leu Asn Met Thr Ser
 305 310 315 320

Ala Lys Ile Ile Ser Phe Leu Leu Pro Pro Asp Glu Ser Leu His Ser
 325 330 335

Leu Gln Ser Arg Ile Glu Arg Glu Thr Gly Ile Asn Thr Gly Ser Gln
 340 345 350

Glu Leu Leu Ser Glu Thr Gly Ile Ser Leu Asp Pro Arg Lys Pro Ala
 355 360 365

Ser Gln Cys Val Leu Asp Gly Val Arg Gly Cys Asp Ser Tyr Met Val
 370 375 380

Tyr Leu Phe Asp Lys Ser Lys Thr Val Tyr Glu Gly Pro Phe Ala Ser
 385 390 395 400

Arg Ser Leu Ser Asp Cys Val Asn Tyr Ile Val Gln Asp Ser Lys Ile
 405 410 415

Gln Leu Pro Ile Ile Gln Leu Arg Lys Val Trp Ala Glu Ala Val His
 420 425 430

Tyr Val Ser Gly Leu Lys Glu Asp Tyr Ser Arg Leu Phe Gln Gly Gln
 435 440 445

Arg Ala Ala Met Leu Ser Leu Leu Arg Tyr Asn Ala Asn Leu Thr Lys
 450 455 460

Met Lys Asn Thr Leu Ile Ser Ala Ser Gln Gln Leu Lys Ala Lys Leu
 465 470 475 480

Glu Phe Phe His Lys Ser Ile Gln Leu Asp Leu Glu Arg Tyr Ser Glu
 485 490 495

Gln Met Thr Tyr Gly Ile Ser Ser Glu Lys Met Leu Lys Ala Trp Lys
 500 505 510

Glu Met Glu Glu Lys Ala Ile His Tyr Ala Glu Val Gly Val Ile Gly
 515 520 525

Tyr Leu Glu Asp Gln Ile Met Ser Leu His Ala Glu Ile Met Glu Leu
 530 535 540

Gln Lys Ser Pro Tyr Gly Arg Arg Gln Gly Asp Leu Met Glu Ser Leu
 545 550 555 560

Glu Gln Arg Ala Ile Asp Leu Tyr Lys Gln Leu Lys His Arg Pro Ser
 565 570 575

Asp His Ser Tyr Ser Asp Ser Thr Glu Met Val Lys Ile Ile Val His
 580 585 590

Thr Val Gln Ser Gln Asp Arg Val Leu Lys Glu Leu Phe Gly His Leu
 595 600 605

Ser Lys Leu Leu Gly Cys Lys Gln Lys Ile Ile Asp Leu Leu Pro Lys
 610 615 620

Val Glu Val Ala Leu Ser Asn Ile Lys Glu Ala Asp Asn Thr Val Met
 625 630 635 640

Phe Met Gln Gly Lys Arg Gln Lys Glu Ile Trp His Leu Leu Lys Ile
 645 650 655

Ala Cys Thr Gln Ser Ser Ala Arg Ser Leu Val Gly Ser Ser Leu Glu
 660 665 670

Gly Ala Val Thr Pro Gln Thr Ser Ala Trp Leu Pro Pro Thr Ser Ala
 675 680 685

Glu His Asp His Ser Leu Ser Cys Val Val Thr Pro Gln Asp Gly Glu

690		695		700
Thr Ser Ala Gln Met Ile Glu Glu Asn Leu Asn Cys Leu Gly His Leu				
705		710		715 720
Ser Thr Ile Ile His Glu Ala Asn Glu Glu Gln Gly Asn Ser Met Met				
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Asn Leu Asp Trp Ser Trp Leu Thr Glu				
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Met Arg Glu Arg Leu Gly Thr Gly Gly Phe Gly Asn Val Cys Leu Tyr				
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Gln His Arg Glu Leu Asp Leu Lys Ile Ala Ile Ala Ser Cys Arg Leu				
	35		40	45
Glu Leu Ser Thr Lys Asn Arg Glu Arg Trp Cys His Glu Ile Gln Ile				
	50		55	60
Met Lys Lys Leu Asn His Ala Asn Val Val Lys Ala Cys Asp Val Pro				
65	70		75	80
Glu Glu Leu Asn Ile Leu Ile His Asp Val Pro Leu Leu Ala Met Glu				
	85		90	95
Tyr Cys Ser Gly Gly Asp Leu Arg Lys Leu Leu Asn Lys Pro Glu Asn				
	100		105	110
Cys Cys Gly Leu Lys Glu Ser Gln Ile Leu Ser Leu Leu Ser Asp Ile				
	115		120	125
Gly Ser Gly Ile Arg Tyr Leu His Glu Asn Lys Ile Ile His Arg Asp				
	130		135	140

Leu Lys Pro Glu Asn Ile Val Leu Gln Asp Val Gly Gly Lys Ile Ile
 145 150 155 160

His Lys Ile Ile Asp Leu Gly Tyr Ala Lys Asp Val Asp Gln Gly Ser
 165 170 175

Leu Cys Thr Ser Phe Val Gly Thr Leu Gln Tyr Leu Ala Pro Glu Leu
 180 185 190

Phe Glu Asn Lys Pro Tyr Thr Ala Thr Val Asp Tyr Trp Ser Phe Gly
 195 200 205

Thr Met Val Phe Glu Cys Ile Ala Gly Tyr Arg Pro Phe Leu His His
 210 215 220

Leu Gln Pro Phe Thr Trp His Glu Lys Ile Lys Lys Lys Asp Pro Lys
 225 230 235 240

Cys Ile Phe Ala Cys Glu Glu Met Ser Gly Glu Val Arg Phe Ser Ser
 245 250 255

His Leu Pro Gln Pro Asn Ser Leu Cys Ser Leu Ile Val Glu Pro Met
 260 265 270

Glu Asn Trp Leu Gln Leu Met Leu Asn Trp Asp Pro Gln Gln Arg Gly
 275 280 285

Gly Pro Val Asp Leu Thr Leu Lys Gln Pro Arg Cys Phe Val Leu Met
 290 295 300

Asp His Ile Leu Asn Leu Lys Ile Val His Ile Leu Asn Met Thr Ser
 305 310 315 320

Ala Lys Ile Ile Ser Phe Leu Leu Pro Pro Asp Glu Ser Leu His Ser
 325 330 335

Leu Gln Ser Arg Ile Glu Arg Glu Thr Gly Ile Asn Thr Gly Ser Gln
 340 345 350

Glu Leu Leu Ser Glu Thr Gly Ile Ser Leu Asp Pro Arg Lys Pro Ala
 355 360 365

Ser Gln Cys Val Leu Asp Gly Val Arg Gly Cys Asp Ser Tyr Met Val

370		375		380
Tyr 385	Leu Phe Asp Lys Ser 390	Lys Thr Val Tyr 395	Glu Gly Pro Phe Ala Ser 400	
Arg 405	Ser Leu Ser Asp Cys Val Asn Tyr 410	Ile Val Gln Asp Ser 415	Lys Ile	
Gln 420	Leu Pro Ile Ile Gln Leu Arg Lys 425	Val Trp Ala Glu Ala Val His 430		
Tyr 435	Val Ser Gly Leu Lys Glu Asp Tyr Ser Arg Leu Phe Gln Gly Gln 445			
Arg 450	Ala Ala Met Leu Ser Leu Leu Arg Tyr Asn Ala Asn Leu Thr Lys 455			
Met 465	Lys Asn Thr Leu Ile Ser Ala Ser Gln Gln Leu Lys Ala Lys Leu 470			
Glu 485	Phe Phe His Lys Ser Ile Gln Leu Asp Leu Glu Arg Tyr Ser Glu 490			
Gln 500	Met Thr Tyr Gly Ile Ser Ser Glu Lys Met Leu Lys Ala Trp Lys 505			
Glu 515	Met Glu Glu Lys Ala Ile His Tyr Ala Glu Val Gly Val Ile Gly 520			
Tyr 530	Leu Glu Asp Gln Ile Met Ser Leu His Ala Glu Ile Met Glu Leu 535			
Gln 545	Lys Ser Pro Tyr Gly Arg Arg Gln Gly Asp Leu Met Glu Ser Leu 550			
Glu 565	Gln Arg Ala Ile Asp Leu Tyr Lys Gln Leu Lys His Arg Pro Ser 570			
Asp 580	His Ser Tyr Ser Asp Ser Thr Glu Met Val Lys Ile Ile Val His 585			
Thr 595	Val Gln Ser Gln Asp Arg Val Leu Lys Glu Leu Phe Gly His Leu 600			

Ser Lys Leu Leu Gly Cys Lys Gln Lys Ile Ile Asp Leu Leu Pro Lys
610 615 620

Val Glu Val Ala Leu Ser Asn Ile Lys Glu Ala Asp Asn Thr Val Met
625 630 635 640

Phe Met Gln Gly Lys Arg Gln Lys Glu Ile Trp His Leu Leu Lys Ile
645 650 655

Ala Cys Thr Gln Ser Ser Ala Arg Ser Leu Val Gly Ser Ser Leu Glu
660 665 670

Gly Ala Val Thr Pro Gln Thr Ser Ala Trp Leu Pro Pro Thr Ser Ala
675 680 685

Glu His Asp His Ser Leu Ser Cys Val Val Thr Pro Gln Asp Gly Glu
690 695 700

Thr Ser Ala Gln Met Ile Glu Glu Asn Leu Asn Cys Leu Gly His Leu
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Ser Thr Ile Ile His Glu Ala Asn Glu Glu Gln Gly Asn Ser Met Met
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Asn Leu Asp Trp Ser Trp Leu Thr Glu
740 745

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<400> 26

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Gln Arg Glu Asn Pro Pro Gly Pro Pro Ile Ala Ala Ser Ala Pro Gly
35 40 45

Pro Ser Gln Ser Leu Gly Leu Asn Val His Asn Met Thr Pro Ala Thr
50 55 60

Ser Pro Ile Gly Ala Ser Gly Val Ala His Arg Ser Gln Ser Ser Glu
 65 70 75 80

Gly Val Ser Ser Leu Ser Ser Ser Pro Ser Asn Ser Leu Glu Thr Gln
 85 90 95

Ser Gln Ser Leu Ser Arg Ser Gln Ser Met Asp Ile Asp Gly Val Ser
 100 105 110

Cys Glu Lys Ser Met Ser Gln Val Asp Val Asp Ser Gly Ile Glu Asn
 115 120 125

Met Glu Val Asp Glu Asn Asp Arg Arg Glu Lys Arg Ser Leu Ser Asp
 130 135 140

Lys Glu Pro Ser Ser Gly Pro Glu Val Ser Glu Glu Gln Ala Leu Gln
 145 150 155 160

Leu Val Cys Lys Ile Phe Arg Val Ser Trp Lys Asp Arg Asp Arg Asp
 165 170 175

Val Ile Phe Leu Ser Ser Leu Ser Ala Gln Phe Lys Gln Asn Pro Lys
 180 185 190

Glu Val Phe Ser Asp Phe Lys Asp Leu Ile Gly Gln Ile Leu Met Glu
 195 200 205

Val Leu Met Met Ser Thr Gln Thr Arg Asp Glu Asn Pro Phe Ala Ser
 210 215 220

Leu Thr Ala Thr Ser Gln Pro Ile Ala Ala Ala Arg Ser Pro Asp
 225 230 235 240

Arg Asn Leu Leu Leu Asn Thr Gly Ser Asn Pro Gly Thr Ser Pro Met
 245 250 255

Phe Cys Ser Val Ala Ser Phe Gly Ala Ser Ser Leu Ser Ser Leu Gly
 260 265 270

Ala Ser Gly Gly Ala Ser Asn Trp Asp Ser Tyr Ser Asp His Phe Thr
 275 280 285

Ile Glu Thr Cys Lys Glu Thr Asp Met Leu Asn Tyr Leu Ile Glu Cys
 290 295 300

Phe Asp Arg Val Gly Ile Glu Glu Lys Lys Ala Pro Lys Met Cys Ser
 305 310 315 320

Gln Pro Ala Val Ser Gln Leu Leu Ser Asn Ile Arg Ser Gln Cys Ile
 325 330 335

Ser His Thr Ala Leu Val Leu Gln Gly Ser Leu Thr Gln Pro Arg Ser
 340 345 350

Leu Gln Gln Pro Ser Phe Leu Val Pro Tyr Met Leu Cys Arg Asn Leu
 355 360 365

Pro Tyr Gly Phe Ile Gln Glu Leu Val Arg Thr Thr His Gln Asp Glu
 370 375 380

Glu Val Phe Lys Gln Ile Phe Ile Pro Ile Leu Gln Gly Leu Ala Leu
 385 390 395 400

Ala Ala Lys Glu Cys Ser Leu Asp Ser Asp Tyr Phe Lys Tyr Pro Leu
 405 410 415

Met Ala Leu Gly Glu Leu Cys Glu Thr Lys Phe Gly Lys Thr His Pro
 420 425 430

Val Cys Asn Leu Val Ala Ser Leu Arg Leu Trp Leu Pro Lys Ser Leu
 435 440 445

Ser Pro Gly Cys Gly Arg Glu Leu Gln Arg Leu Ser Tyr Leu Gly Ala
 450 455 460

Phe Phe Ser Phe Ser Val Phe Ala Glu Asp Asp Val Lys Val Val Glu
 465 470 475 480

Lys Tyr Phe Ser Gly Pro Ala Ile Thr Leu Glu Asn Thr Arg Val Val
 485 490 495

Ser Gln Ser Leu Gln His Tyr Leu Glu Leu Gly Arg Gln Glu Leu Phe
 500 505 510

Lys Ile Leu His Ser Ile Leu Leu Asn Gly Glu Thr Arg Glu Ala Ala
 515 520 525

Leu Ser Tyr Met Ala Ala Val Val Asn Ala Asn Met Lys Lys Ala Gln
 530 535 540

Met Gln Thr Asp Asp Arg Leu Val Ser Thr Asp Gly Phe Met Leu Asn
 545 550 555 560

Phe Leu Trp Val Leu Gln Gln Leu Ser Thr Lys Ile Lys Leu Glu Thr
 565 570 575

Val Asp Pro Thr Tyr Ile Phe His Pro Arg Cys Arg Ile Thr Leu Pro
 580 585 590

Asn Asp Glu Thr Arg Val Asn Ala Thr Met Glu Asp Val Asn Asp Trp
 595 600 605

Leu Thr Glu Leu Tyr Gly Asp Gln Pro Pro Phe Ser Glu Pro Lys Phe
 610 615 620

Pro Thr Glu Cys Phe Phe Leu Thr Leu His Ala His His Leu Ser Ile
 625 630 635 640

Leu Pro Ser Cys Arg Arg Tyr Ile Arg Arg Leu Arg Ala Ile Arg Glu
 645 650 655

Leu Asn Arg Thr Val Glu Asp Leu Lys Asn Asn Glu Ser Gln Trp Lys
 660 665 670

Asp Ser Pro Leu Ala Thr Arg His Arg Glu Met Leu Lys Arg Cys Lys
 675 680 685

Thr Gln Leu Lys Lys Leu Val Arg Cys Lys Ala Cys Ala Asp Ala Gly
 690 695 700

Leu Leu Asp Glu Ser Phe Leu Arg Arg Cys Leu Asn Phe Tyr Gly Leu
 705 710 715 720

Leu Ile Gln Leu Leu Leu Arg Ile Leu Asp Pro Ala Tyr Pro Asp Ile
 725 730 735

Thr Leu Pro Leu Asn Ser Asp Val Pro Lys Val Phe Ala Ala Leu Pro
 740 745 750

Glu Phe Tyr Val Glu Asp Val Ala Glu Phe Leu Phe Phe Ile Val Gln
 755 760 765

Tyr Ser Pro Gln Ala Leu Tyr Glu Pro Cys Thr Gln Asp Ile Val Met

770		775		780
Phe Leu Val Val Met	Leu Cys Asn Gln Asn Tyr	Ile Arg Asn Pro Tyr		
785	790	795	800	
Leu Val Ala Lys	Leu Val Glu Val Met	Phe Met Thr Asn Pro	Ala Val	
	805	810	815	
Gln Pro Arg Thr	Gln Lys Phe Phe Glu Met	Ile Glu Asn His Pro	Leu	
	820	825	830	
Ser Thr Lys	Leu Leu Val Pro	Ser Leu Met Lys Phe Tyr	Thr Asp Val	
	835	840	845	
Glu His Thr Gly	Ala Thr Ser Glu Phe Tyr Asp	Lys Phe Thr Ile Arg		
850	855	860		
Tyr His Ile Ser Thr	Ile Phe Lys Ser Leu Trp	Gln Asn Ile Ala His		
865	870	875	880	
His Gly Thr Phe	Met Glu Glu Phe Asn Ser	Gly Lys Gln Phe Val Arg		
	885	890	895	
Tyr Ile Asn Met	Leu Ile Asn Asp Thr Thr	Phe Leu Leu Asp Glu Ser		
	900	905	910	
Leu Glu Ser	Leu Lys Arg Ile His Glu Val	Gln Glu Glu Met Lys Asn		
915	920	925		
Lys Glu Gln Trp Asp	Gln Leu Pro Arg Asp	Gln Gln Gln Ala Arg Gln		
930	935	940		
Ser Gln Leu Ala Gln	Asp Glu Arg Val Ser Arg	Ser Tyr Leu Ala Leu		
945	950	955	960	
Ala Thr Glu Thr	Val Asp Met Phe His Ile	Leu Thr Lys Gln Val Gln		
	965	970	975	
Lys Pro Phe	Leu Arg Pro Glu Leu Gly	Pro Arg Leu Ala Ala Met Leu		
	980	985	990	
Asn Phe Asn	Leu Gln Gln Leu Cys Gly	Pro Lys Cys Arg Asp Leu Lys		
995	1000	1005		

Val	Glu	Asn	Pro	Glu	Lys	Tyr	Gly	Phe	Glu	Pro	Lys	Lys	Leu	Leu
1010						1015					1020			
Asp	Gln	Leu	Thr	Asp	Ile	Tyr	Leu	Gln	Leu	Asp	Cys	Ala	Arg	Phe
1025						1030					1035			
Ala	Lys	Ala	Ile	Ala	Asp	Asp	Gln	Arg	Ser	Tyr	Ser	Lys	Glu	Leu
1040						1045					1050			
Phe	Glu	Glu	Val	Ile	Ser	Lys	Met	Arg	Lys	Ala	Gly	Ile	Lys	Ser
1055						1060					1065			
Thr	Ile	Ala	Ile	Glu	Lys	Phe	Lys	Leu	Leu	Ala	Glu	Lys	Val	Glu
1070						1075					1080			
Glu	Ile	Val	Ala	Lys	Asn	Ala	Arg	Ala	Glu	Ile	Asp	Tyr	Ser	Asp
1085						1090					1095			
Ala	Pro	Asp	Glu	Phe	Arg	Asp	Pro	Leu	Met	Asp	Thr	Leu	Met	Thr
1100						1105					1110			
Asp	Pro	Val	Arg	Leu	Pro	Ser	Gly	Thr	Ile	Met	Asp	Arg	Ser	Ile
1115						1120					1125			
Ile	Leu	Arg	His	Leu	Leu	Asn	Ser	Pro	Thr	Asp	Pro	Phe	Asn	Arg
1130						1135					1140			
Gln	Thr	Leu	Thr	Glu	Ser	Met	Leu	Glu	Pro	Val	Pro	Glu	Leu	Lys
1145						1150					1155			
Glu	Gln	Ile	Gln	Ala	Trp	Met	Arg	Glu	Lys	Gln	Asn	Ser	Asp	His
1160						1165					1170			